CBER Update:
Advertising and Promotional Labeling Branch (APLB)

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Division of Case Management
Office of Compliance and Biologics Quality

RAPS Advertising, Promotion & Labeling Conference
2-3 June 2005

Agenda

- Overview of APLB
- Looking Back...an Enforcement Review
- Practical Advice
- Looking Ahead...

Creativity never ceases to amaze!

U.S.: No billboards in space

WASHINGTON (Reuters) -- The U.S. government does not want billboards in space.

The Federal Aviation Administration proposed Thursday to amend its regulations to ensure that it can enforce a law that prohibits "obtrusive" advertising in zero gravity.

"Objects placed in orbit, if large enough, could be seen by people around the world for long periods of time," the FAA said in a regulatory filing.

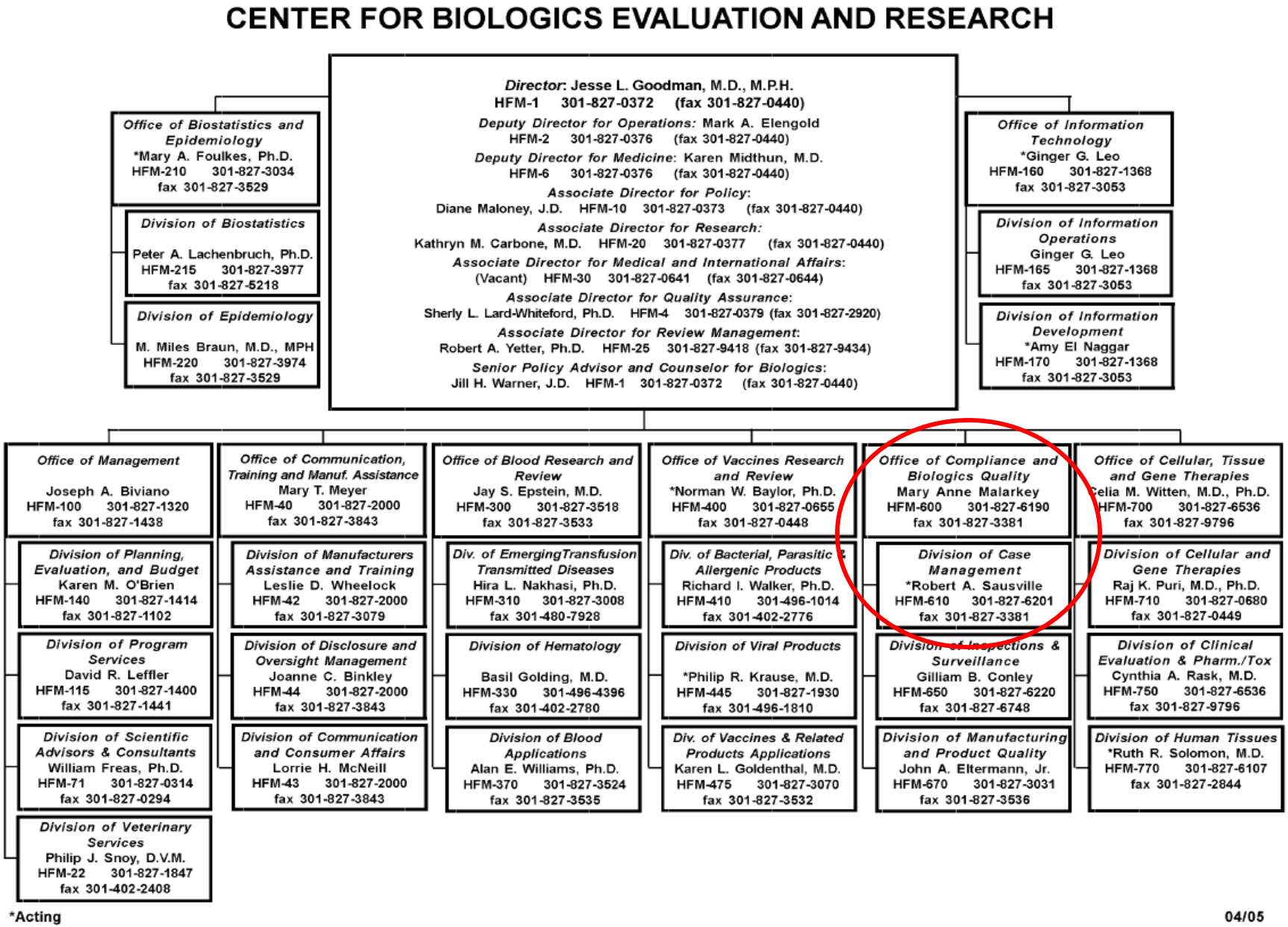
Currently, the FAA lacks the authority to enforce the existing law.

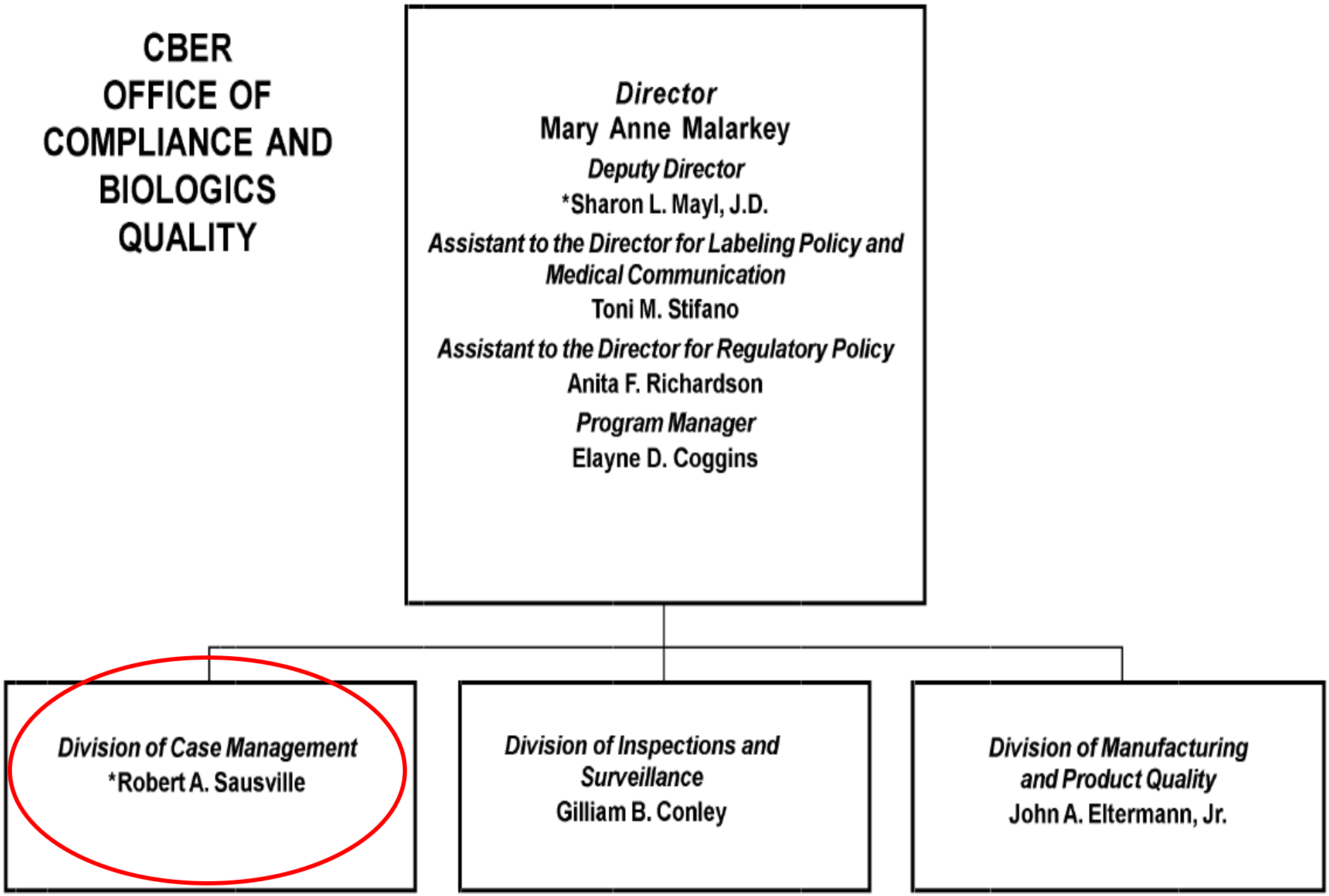
For instance, outsized billboards deployed by a space company into low Earth orbit could appear as large as the moon and be seen without a telescope, the FAA said. Big and bright advertisements might hinder astronomers.

"Large advertisements could destroy the darkness of the night sky," regulators said.

May 2005

CBER Organization

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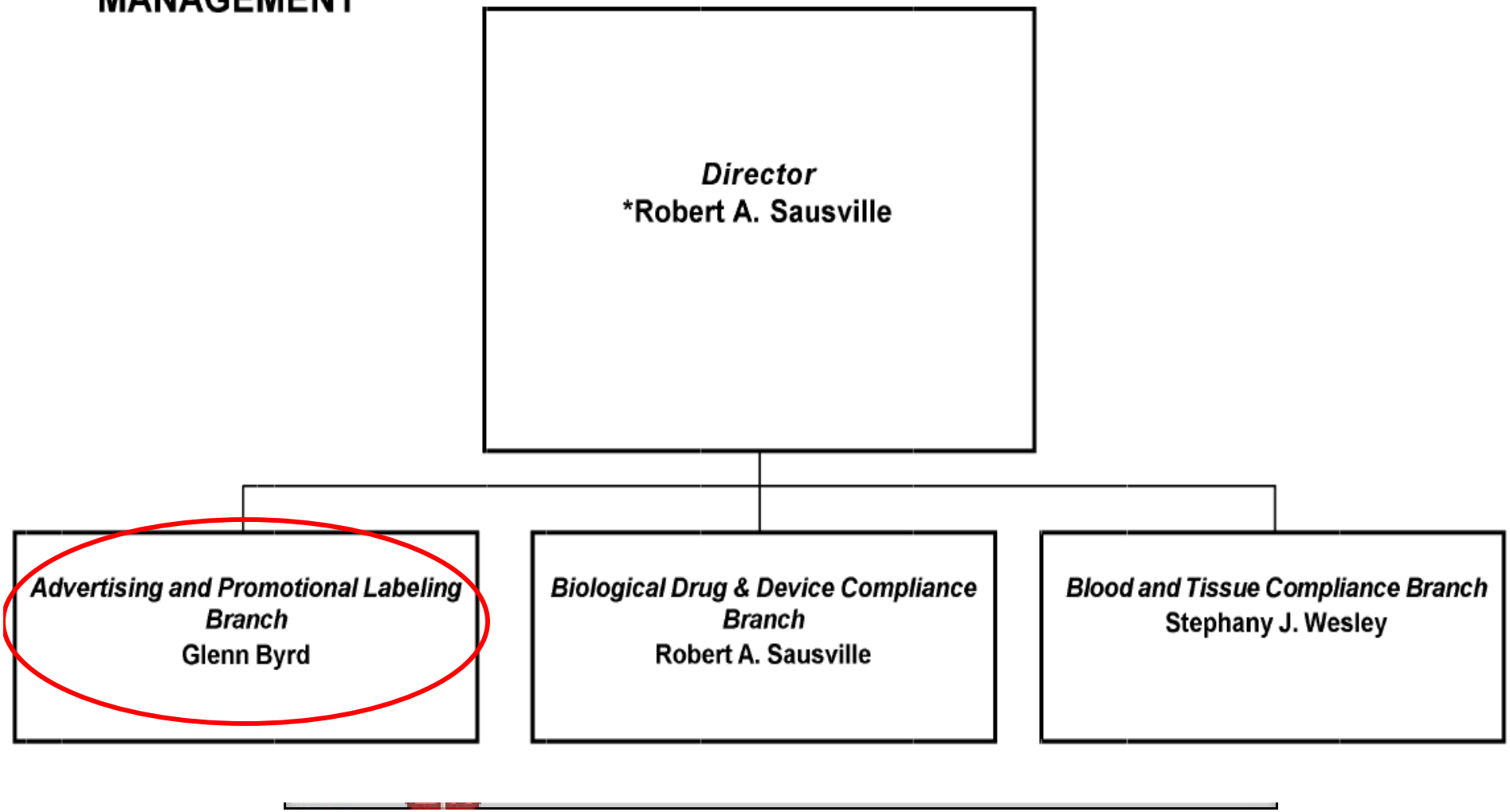


APLB Staff

- Glenn Byrd, MBA, RAC – Branch Chief
- CDR Nancy Chamberlin, Pharm.D.
- Maryann Gallagher
- Yongkai Weng, Ph.D.
- Beverly Conner, Pharm.D.

Looking Back...

An Enforcement Review

APLB Advisory Actions 6/04 – 5/05

- Untitled Letters – three (3) issued
  - Vivotif – Berna Biotech (6/04)
  - Helixate FS – Bayer HealthCare (8/04)
  - WinRho – Cangene Corp. (1/05)

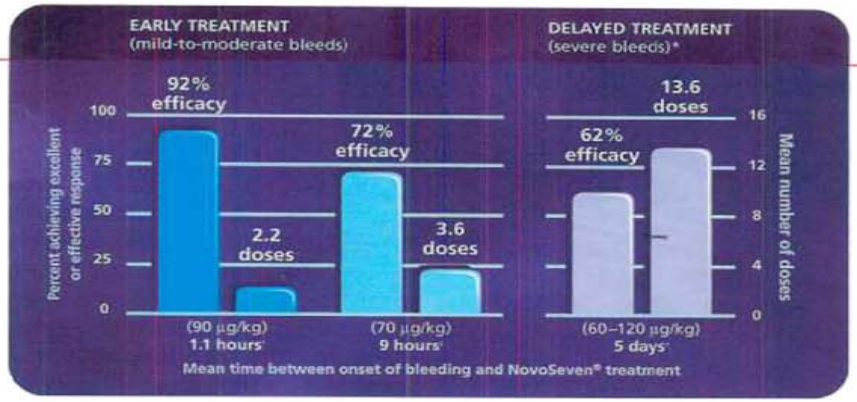
APLB Advisory Actions 6/04 – 5/05

- Warning Letters – eight (8) issued
  - Engerix-B, Havrix, Twinrix – GlaxoSmithKline Biologics (7/04)
  - NovoSeven – Novo Nordisk Pharmaceuticals (8/04)
  - Rhophylac – ZLB Bioplasma (9/04)
  - Zemaira – Aventis Behring (10/04)
  - DigiFab – Protherics, Inc. (11/04)
  - Nabi-Hb – Nabi Biopharmaceuticals (1/05)
  - Flebogamma – Instituto Grifols (3/05)
- All CBER Enforcement letters are posted at: www.fda.gov/cber/efoi/adpromo.htm

For the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to FVIII or FIX

NovoSeven®:
Clinical advantages with early treatment

3 NovoSeven® studies of treatment for intramuscular bleeds[1-3]



* NovoSeven® used as salvage therapy.

Three separate studies analyzed a total of 245 peripheral intramuscular bleeding episodes. Time from onset of bleed until first treatment, dosage, number of doses, and responses were recorded for each study. Enrolled subjects had hemophilia A or B with inhibitors (several patients in the late treatment study had acquired inhibitors; several patients in the early treatment study [treatment after 9 hours] had hemophilia without inhibitors).

> **"...data suggest that in >90% of cases... early administration of rFVIIa achieves haemostasis after 1 to 3 injections. In more than 90% of responders, haemostasis is maintained for at least 24 h."**[1]
>
> —*Key NS et al, 1998*

- **Early administration of coagulation factor in patients with bleeding episodes can reduce pain and the risk of arthritis and permanent disability**[4]

novo nordisk®

NovoSeven®
Coagulation Factor VIIa (Recombinant)
Tab 2
The recombinant clamp

Rhophylac®
Rh$_0$(D) Immune Globulin Intravenous (Human)
Purity delivered

ZLB Behring

The Rhophylac® Advantage

Your doctor has prescribed Rhophylac® because of its unique benefits:

- Rhophylac® is convenient to use because it can be given 2 ways - through an intravenous (IV) line, which many patients find more comfortable, or by injection into a muscle (IM)
- Rhophylac® is a very safe, highly pure product, prepared at a modern, state-of-the-art facility
- Rhophylac® is thimerosal-free, mercury-free, and latex-free

If you are among the one in ten mothers who is Rh-negative, your doctor will talk to you about a serious but treatable condition, known as hemolytic disease of the newborn (HDN), that could impact the health of your baby and your ability to have more children in the future. It will be very important for you to consider taking Rhophylac®, a special treatment that can help protect you and your baby from harm.

Rhophylac® is a specially prepared product given to women with Rh-negative blood during pregnancies when the father has Rh-positive blood. It is generically known as Rho(D) Immunoglobulin Intravenous (Human), or "RhIg" for short. Like all RhIg therapies, Rhophylac® is made from human plasma; Rhophylac® is made through a unique purification process that ensures it is highly pure. Rhophylac® is designed to prevent HDN by removing the Rh-positive blood cells that can cause a woman's immune system to develop antibodies. It is also used in mismatched blood transfusions.

Although all RhIg products are given as shots, Rhophylac®is the only RhIg made by the ChromaPlus process. Not only does ChromaPlus allows for administration options that make Rhophylac® more comfortable and faster acting than a traditional RhIg shot, but it also ensures that the RhIg is highly pure and unparalleled for safety.

This site is currently under construction and new tools and resources are being added every day. Please check back again soon!

As with all plasma-derived products, Rhophylac® may contain infectious agents such as viruses that can cause disease. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is considered extremely remote.

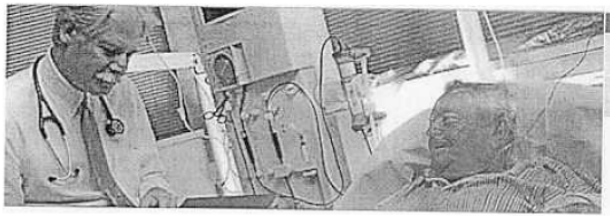
For more information, please see full Prescribing Information and List of References.

NABI BIOPHARMACEUTICALS

ABOUT US PIPELINE PRODUCTS

POWERING THE IMM

PATIENTS
Patients Overview
Product Information
PhosLo®
Nabi-HB®
WinRho SDF®
Aloprim™
Plasma Products
Vision, Mission and Values



HOME SEAR
PATIENTS
MEDIA

Patients

Welcome to Nabi Biopharmaceuticals' patient area. Nabi Biopharmaceuticals specializes in developing biopharmaceutical products that address serious, unmet medical needs in the areas of infectious, autoimmune and addictive diseases.

This patient area is designed to help you learn more about the company's four marketed products:

- PhosLo® (calcium acetate) Gelcaps and Tablets are used for the control of hyperphosphatemia (elevated serum phosphorus levels) in patients with end-stage renal (kidney) failure.
- Nabi-HB® [Hepatitis B Immune Globulin (Human)] is a hyperimmune globulin used to treat patients acutely exposed to blood containing the hepatitis B virus (HBV).
- WinRho SDF® [Rho(D) Immune Globulin Intravenous (Human)] is a hyperimmune globulin used for the treatment of ITP, an autoimmune disorder affecting platelets.
- Aloprim™(Allopurinol sodium) for Injection is used for the management of patients with leukemia, lymphoma, and solid tumor malignancies who are receiving cancer therapy which causes elevations of serum and urinary uric acid levels and who cannot tolerate oral therapy.

Code No. 10340-00-GEN-130704

 Site Map | Glossary of Terms | Terms and Conditions of Use

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Nabi-HB® Hepatitis B Immune Globulin (Human)

Nabi-HB® (Hepatitis B Immune Globulin [Human]) is an immune globulin that contains antibodies to hepatitis B surface antigen (anti-HBs). In contrast to vaccination, which provides long-term immunity to hepatitis B, Nabi-HB provides passive immunization (i.e. short-term protection) following exposure to hepatitis B virus. Nabi-HB is indicated for the treatment of:

- acute exposure to blood containing hepatitis B surface antigen (HBsAg)
- perinatal exposure of infants born to HBsAg-positive mothers
- sexual exposure to HBsAg-positive persons
- household exposure to persons with acute HBV infection.

Code No. 10570-42-HEP-150704

RESOURCES
Full Prescribing I
Nabi-HB
Hepatitis B Reso

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The APLB Top Seven Problem List

5. False information on approved indications and limitations of other marketed products
6. Promotion of broader indication than approved
7. Promotion that product is more effective based on timing of drug administration in the absence of substantial evidence

The APLB Top Seven Problem List

1. Omission of risk information
2. Failure to submit materials to FDA
3. Claims of “unsurpassed...safety”
4. Claims regarding the reduction in frequency or severity of adverse events or clinical symptoms in the absence of substantial evidence

Practical Advice

- When developing/approving promotional pieces:
  - ✓Fair Balance risk information should be included in the body of the piece
  - ✓It is not sufficient to simply attach the PI or the brief summary
  - ✓Submit a copy to FDA at the same time you distribute the pieces

Corrective Actions

- Warning letters – firms are requested to develop a plan of action to distribute corrective information to audience that received violative information
  - We have been consistent in this corrective action requirement
  - Because of the nature of the violation, the corrective message should be pro-active

Corrective Actions (cont'd)

- Examples:
  - Conferences – send corrective letters to all conference attendees
  - Journals – send corrective letters to all subscribers or publish a corrective ad in journal(s)
  - Website – post correction on the website page(s)

Looking Ahead...

- Electronic Submission of 2253 Materials
- New guidance documents – draft and final
- Continued vigorous enforcement
- Continue working interactively with industry to achieve voluntary compliance

Looking Ahead...

- Electronic submissions for FDA Form-2253 materials.
  - ✓ Similar to the January 2001 draft guidance on electronic submissions for ad/promo materials
  - ✓ Presently, we receive CDs with one paper 2253 from some companies instead of all paper
  - ✓ Fully electronic submissions through the CBER electronic document room within the year

Looking Ahead...

- Guidance Documents
  - ✓Help-Seeking/Disease Awareness
  - ✓Brief Summary Guidance
  - ✓Outdoor Media
  - ✓Presentation of Risk Information
  - ✓Electronic Submissions

APLB Contact Information

- Phone: 301-827-3028
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- www.fda.gov/cber/efoi/adpromo.htm